26. (Amended) The method of claim 20, wherein the erythropoietin[, erythropoietin derivative, erythropoietin mutant or fragments thereof,] is of recombinant origin.

Please cancel claims 27-29 without prejudice.

## REMARKS

The amendments to the claims are supported by claims 1-14 as filed.

The amendments are aimed at more particularly pointing out and claiming the subject matter of the present invention.

Since the amendments do not require any new search and no new issue is raised by the amendments, entry of the amendments is respectfully requested.

Claims 15-30 are pending. However, because claim 11 was inadvertently numbered claim 12 in the Preliminary Amendment filed on May 5, 1997, the Examiner renumbered claims 15-30 as claims 14-29, so claims 14-29 were pending. With the cancellation of claims 27-29, 14-26 are pending.

### Information Disclosure Statement

Despite that fact that the response filed September 30, 1998 requests that the Examiner acknowledged the consideration of the Information Disclosure Statement filed on May 5, 1997, the Final Office Action does not indicate whether the Information Disclosure Statement was considered by the Examiner. The Examiner is requested

again to consider the Information Disclosure Statement and send applicant a copy with his initials.

Finality of the Office Action

The office action dated December 21, 1998 was made Final. It is noted, however, that two rejections (the nonenablement rejection of claims 14-29 and the anticipatory rejection of claims 14-29) that are made the first time in this Final Office Action were not made in the First Office Action and yet these rejections could have been made in the First Office Action (because the issues were there). Therefore, the Final Office Action is incorrect by asserting that these two new rejections were necessitated by the amendment filed in response to the First Office Action. Under U.S. patent practice, applicants are entitled to two opportunities in rebutting a rejection unless the issue was introduced by applications after receiving the first office action. Applicant requests the Examiner withdraw the finality of the office action dated December 21, 1998.

Claim Rejections – 35 U.S.C. 112, First Paragraph

Claims 14-29 were rejected because the Final Office Action asserts that the disclosure fails to adequately teach how to use the claimed methods based on two reasons. Applicant respectfully traverses the rejection.

I. Fragments, Derivatives and Mutants of EPO

The Office Action asserts that one skilled in the art would not be able to identify, without undue experimentation, EPO fragments without the specification disclosing the desired functional activity and disclosing the conserved structure. The Office Action states that the artisan would have to determine all the known and unknown functional activities of EPO and then to determine which compounds had similar activities. Applicant respectfully disagrees that the specification fails to disclose the desired functional activity and the artisan would have to determine all the known and unknown functional activities of EPO. This is because page 3, the fourth paragraph, discloses that any EPO derivatives, mutants or fragments thereof that (1) are nonimmunogenic upon administration and (2) have an ameliorating effect on chronic inflammation would be effective in the claimed methods. Therefore, the artisan is required to determine only one functional activity of EPO, i.e. amelioration of chronic inflammation, which can be determined with a reasonable amount of experimentation. Applicant notes that only a reasonable amount of experimentation would be required for the artisan to determine whether a compound is a EPO derivative, mutant or fragment that works in the claimed method (by looking for only two biological properties: (1) being nonimmunogenic upon administration and (2) having an ameliorating effect on chronic inflammation).

The Office Action asserts that the specification does not disclose the conserved structure and the Office Action cites the paper by Smilek that even minor change in the structure of a biologically active molecule can have drastic effects on function activity. Applicant respectfully disagrees. Smilek's paper is not relevant because Smilek deals

with only a myelin basic protein which is very different from EPO both functionally and structurally.

Although the instant claims are fully enabled, in order to advance prosecution, applicant deletes "an erythropoietin derivative, erythropoietin mutant or fragments thereof" from claims 14, 18, 20, 22, 24 and 26 and also cancels claims 27-29. Withdrawal of the nonenablement rejection is requested.

II. Autoimmune Disease, Scope

Claims 14-29 were rejected because the Final Office Action asserts that the specification fails to teach one skilled in the art how to use the claimed methods to treat diseases other than rheumatoid arthritis using EPO due to the complexity of the physiological mechanisms of different antoimmune diseases. Applicant respectfully traverses the rejection.

First, claims 17-20 and 23-26 are directed to the treatment of the chronic inflammation, symptoms or a disease activity of rheumatoid arthrities. Since the Final Office Action already states that EPO is effective in treating rheumatoid arthritis, the nonenablement rejection of claims 17-20 and 23-26 should be withdrawn now that "an erythropoietin derivative, erythropoietin mutant or fragments thereof" is deleted from these claims.

Second, the Final Office Action makes an erroneous characterization of the methods claimed. Claims 14-16, 21 and 22 are directed to methods of treating chronic inflammation, which inflammation could be associated with an immune disease or auto-

immune disease (and claims 17-20 and 23-26 are directed to chronic inflammation, symptoms or a disease activity of rheumatoid arthritis as discussed above). However, the Final Office Action erroneously assumes claims 14-17, 22 and 23 to be directed to a method of treating immune diseases or auto-immune diseases, but actually the methods of claims 14-17, 22 and 23 are for treating chronic inflammation. The Final Office Action already admits that EPO affects the cytokine levels. Pages 4 and 5 of the specification disclose that EPO induces a $T_{h2}$ cytokine secretion profile. It is well known that cytokines play an important role in mediating the chronic inflammatory response. Page 5 of the specification discloses that EPO counteracts the activity of tumor necrosis factor-alpha, which is an important pro-inflammatory cytokines and EPO reduces the production of neutrophils, which are important in inflammation. Working examples also demonstrate that EPO is effective in treating chronic inflammatory symptoms of rheumatoid arthritis. Therefore, there is sufficient teachings in the specification that the claimed methods are effective in treating chronic inflammation, especially chronic inflammatory symptoms in immune diseases or auto-immune diseases, and to practice the claimed methods would not involve an unreasonable amount of experimentation based on the disclosure and what one skilled in the art already knows. Withdrawal of the nonenablement rejection is respectfully requested.

Claim Rejection – 35 U.S.C. 102(b)

Claims 14-29 were rejected as anticipated by GB 2 171 304 because GB '304 teaches using EPO to treat anemia of rheumatoid arthritis and performance of the

method of GB '304 would inherently treat symptoms, such as joint swelling, pain or inflammation of rheumatoid arthritis. Applicant respectfully traverses the rejection.

GB '304 teaches a method of treating anemia of rheumatoid arthritis by administering human EPO (see page 1, lines 5-7). GB '304 does not teach or suggest using EPO to treat chronic inflammation or to treat morning stiffness, painful and swollen joints, pain, and a loss of grip strength in rheumatoid arthritis. GB '304 does not teach every limitation of the claims, so there is no anticipation of the claims.

There would have been no reason or motivation for one of ordinary skill in the art to administer EPO to treat chronic inflammation. The fact that adminstering a substance to treat disease A would inherently treat disease B never renders obvious a claim directed to a method of using said substance to treat disease B under U.S. patent law. Therefore, claims 14-26 would not have been obvious over GB '304.

Conclusion

With the above amendments and reasoning, applicant respectfully requests that all rejections be withdrawn. Applicant submits that the application is in a condition for allowance.

In case this paper is not timely filed, the undersigned hereby petitions for an appropriate extension of time. In the event that any fees are due in connection with this paper, please charge our Deposit Account No. 14-1060.

Respectfully submitted,
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